Keratitis, Ichthyosis and Deafness Syndrome
-A Case Report and Literature Review
Chin-Ya Yang  Yi-Ju Chen  Jui-Lung Shen

The acronym “KID syndrome” was proposed by Skinner et al. in 1981 to represent keratitis, ichthyosis and deafness. It is a rare syndrome and about 70 cases have been reported. Herein, we report a 28-year-old male with keratoderma, bilateral deafness, total blindness, alopecia and cerebellar hypoplasia. Our patient started to have walking difficulties at the age of 6 and is now bed-ridden. Several huge erythematous plaques with verrucous surface were noted over the lower limbs. Squamous cell carcinoma was suspected clinically and skin pathology revealed only hyperkeratosis and acanthosis. The verrucous plaques improved after treatment with emollient, keratolytics and topical antibiotics. We also reviewed the literature concerning this rare syndrome. (Dermatol Sinica 26: 151-156, 2008)

Key words: Keratitis, Ichthyosis, Deafness, KID syndrome

INTRODUCTION

Keratitis, ichthyosis and deafness (KID) syndrome is a rare disease characterized by erythrokeratoderma, sensorineural hearing loss and vascularizing keratitis. It is a congenital ectodermal disorder without a clear mode of inheritance. More than 70 cases of KID syndrome with associated abnormalities have been reported in world literature. Early diagnosis is important to prevent blindness, deaf-mutism, infections and early detection of squamous cell carcinoma.

CASE REPORT

Our patient was a 28-year-old Taiwanese man who was brought to our clinic for the first time when he was 6 years old. He was born after an uncomplicated pregnancy and a normal delivery. His parents, two brothers and three sisters had no skin abnormalities and were otherwise healthy. At birth, he was noted to have dry and rough skin over the whole body while there was no scalp hair, eyebrows or eyelashes. The patient’s skin became thicker after birth, more prominently over the trunk and extensor surfaces of the knees and elbows. Significant photophobia with enlarging grayish-white dot on each pupil was observed by his parents during the first year of his life. He was also noted to have no response to sound. Although he had an abnormal gait and walked on his toes, he had no difficulties walking or riding a bicycle at the time of his first visit to our clinic.

A series of examinations were performed at that time. Ophthalmologic examination showed vascularizing keratitis and superficial pannus infiltration on corneas.
of both eyes. Audiometry revealed bilateral neurosensory deafness. Skin biopsy showed basket-weave hyperkeratosis, papillomatosis, minimal acanthosis, occasional follicular plugs, and nonspecific inflammatory infiltrate in dermis. Computed tomography of brain disclosed a markedly enlarged cisterna magna and hypoplasia of the middle and lower portions of the cerebellar hemispheres and tonsils. The hypoplasia was more prominent on the left side. He was diagnosed with KID syndrome with cerebellar hypoplasia. He was advised to wear a hearing aid and undergo auditory rehabilitation. However, he was lost to follow-up in the following 22 years due to economic reasons.

Recently, he was brought to our clinic because of several skin tumors over the lower legs. Physical examination revealed generalized dryness with hyperkeratosis of the skin (Fig. 1A) with several hyperkeratotic verrucous cracked plaques with crusts and erosions over the lower legs. (Fig. 1B) His palms and soles showed distinctive, fine, reticulated hyperkeratosis. (Fig. 2A, 2B) Tiny spiny processes with follicular arrangement were seen over the face and scalp. (Fig. 3) Deep furrows on scalp, forehead, cheeks and chin produced a characteristic appearance of premature aging. (Fig. 3) His fingernails were normal without dystrophy. However, all toenails showed yellowish discoloration and subungal hyperkeratotic changes. Hairs in the beard area were normal while scalp hairs, eyebrows, eyelashes and moustache were completely absent. (Fig. 3) In addition to his skin, eye and hearing disorders, we noted that he couldn’t walk and was bed-ridden. Club feet with flexion contracture of upper limbs and knees were noted.

Under the suspicion of squamous cell carcinoma, skin biopsy from a verrucous hyperkeratotic plaque on his right lower leg was performed. Histopathology showed papillomatosis, hyperkeratosis, hypogranulosis and acanthosis over epidermis. No atypical keratinocytes were noted. The dermis was unremarkable. (Fig. 4)

Verrucous hyperkeratotic plaques over lower legs were successfully treated with emollient, keratolytics and topical antibiotics. We also gave acitretin (Neotigason) therapy at a dose of 0.4mg/kg body weight per day for 6 months. However, hyperkeratotic skin
DISCUSSION

KID syndrome is an extremely rare disorder. The first publication of a patient with clinical features of this syndrome was in 1915, when Burns described a 16-year-old body with generalized congenital erythroderma, deafness and keratitis. In 1981, Skinner and associates reviewed 18 similarly affected patients and proposed the acronym “KID syndrome” to represent the characteristic features of keratitis, ichthyosis, and deafness. This designation has been adopted by the majority of authors since then.

Characteristic skin findings in KID syndrome are usually present at birth or in early infancy. The skin becomes thicker and has a coarse-grained appearance. Despite the original acronym, features of keratoderma predominate rather than classic ichthyosis. The well-demarcated, erythematous, hyperkeratotic plaques with verrucous surface are distributed over face and extremities alternating with smoother areas. Hyperkeratotic plaques over the face give patients an appearance of premature aging. Follicular keratoses with spiny projections occur over limbs, scalp and face. Palmoplantar keratoderma with grained leather-like appearance is also characteristic. Histological examination of skin usually shows papillomatosis with basket weave hyperkeratosis. Parakeratosis and follicular plugging has also been described. Ultrastructural studies reveal no significant changes.

The second component required for diagnosis is the presence of congenital sensorineural hearing loss. It is generally bilateral and nonprogressive. However, deafness is often detected later in life when delayed speech development has been noticed. Early diagnosis is important to prevent deaf-mutism.

The ophthalmologic defects, the third feature of KID syndrome, are detected in 95% of patients. It is also the most serious changes over whole body only showed limited improvement. Thus, acitretin (Neotigason) was discontinued.
component because it can progress to total blindness. Most patients develop ophthalmologic difficulties during childhood or early adolescence. Photophobia, irritation, tearing, leukoma, opacity and corneal abrasion have been described in previous reports. Vascularizing keratitis develops later, leading to visual disturbance and blindness.7

An increased frequency of bacterial, fungal and viral skin infections, as well as scabies infestations have been observed.2-8 Otitis media, conjunctivitis, visceral infections, such as bronchopneumonia, gastroenteritis, and even sepsis have been noted.2 However, no underlying immunological abnormalities have been demonstrated and the propensity of these patients to develop infections remains unexplained.

Patients may have an increased risk of squamous cell carcinoma of skin and tongue.2,9-13 There was also a case of malignant fibrous histiocytoma with KID syndrome.14

Most patients have sparse or absent scalp hair, eyebrows and eyelashes.2 Some authors described alopecia as secondary to recurrent scalp infection.3,15 However, there are also cases of congenital alopecia, as in our patient.5,16 Nails may be thickened, deformed, brittle, white, hypoplastic or infrequently may be normal.2 The teeth are normally developed in some patient, but in others show defective dentition and are likely to develop caries.2

Neurologically, most patients are intellectually normal. Few patients were mentally retarded. Other less common manifestations include hypohidrosis, shortening of Achilles tendon, growth delay6 and hypoplasia of mammary glands.3,17 Cerebellar hypoplasia, as in our case, has been described in two patients.10,19 However, none of them had clinical symptoms. As for ataxia, only one case of abasia was reported.2 To our knowledge, there have been no other cases of KID syndrome in which the patient was bed-ridden.

The mode of inheritance is still unclear with most patients described in world literature thought to be sporadic.20 However, both an autosomal dominant form9,21,22 and an autosomal recessive form2 have been reported. The scarcity of familial cases could be explained by the rarity of this syndrome and the low rates of procreation due to severe cutaneous lesions.

Recently, the cause of KID syndrome was identified as a germline missense mutation in the GJB2 (gap junctionβ-2) gene encoding for connexin-26, which is essential for gap function formation in various tissues.14,16 Gap junctions are composed of the alignment of two connexon hemichannels on adjacent cell membranes. Each connexon is built by hexameric oligomerization of connexins.21 Gap junctions formed by connexin 26 are found in many epithelia, including cochlea, palmoplantar epidermis, hair follicles, corneal epithelium, sweat glands and ducts.20 Mutations in the GJB2 gene encoding connexin 26 are detrimental to the function of these tissues, causing non-syndromic sensorineural deafness, palmoplantar keratoderma and hearing impairment, Vohwinkel syndrome and KID syndrome.16,23

This disorder is difficult to treat. Early cochlear implantation with speech therapy and regular ophthalmologic follow-up are required. Topical keratolytics agents provide limited benefit. Antimicrobials and antiseptics may be helpful with cutaneous infections. Systemic retinoids may be considered for severely affected individuals. However, previous reports show controversial results.2 Regular ophthalmologic follow-up is essential due to the possibility of corneal neovascularization24 and exacerbation of keratitis21 with systemic retinoids use. As in our case, systemic retinoids seem to be of little value for the treatment of KID syndrome. Periodical skin examination is necessary as the
occurrence of squamous cell carcinoma has been reported.

REFERENCES

角膜炎-魚鱗癬-耳聾症候群
-病例報告及文獻回顧

楊智雅  陳怡如  沈瑞隆
台中榮民總醫院 皮膚科

“KID症狀群”是由Skinner等人於1981年所提出的縮寫，用來表示此症候群中常見的角膜炎-魚鱗癬-耳聾之表現。這是一個極少見的症候群，約70個病例曾經被報導過。本文報告一個28歲男性，出現皮膚過度角化、雙側聽力喪失、失明、禿髮及小腦萎縮的案例。除了典型的臨床表現之外，此病人於6歲開始出現行走困難的現象，現在則處於臥床的狀態。我們同時發現病人於下肢出現紅色疣狀突起的巨大斑塊，臨床上懷疑是鱗狀細胞癌，而切片結果為角質增厚及棘層變厚。這些疣狀突起的斑塊在給予潤膚劑、角質溶解劑及局部塗抹抗生素後獲得改善。我們同時回顧與此症候群有關的文獻。（中華皮誌：26: 151-156, 2008）